REMARKS

I. Status of Claims

Claims 1-8 and 10-18 were pending in the instant application at the time of the official action. Applicants withdraw claims 2-8 and 10-18 as being directed to unelected subject matter. Applicants request that the requirement to cancel claims 2-8 and 10-18 be held in abeyance until such a time as when Claim 1 is indicated as being allowable, in order to preserve the option to request rejoinder of the method claims at that time.

II. Objection to Specification.

The Official Action noted that the specification did not comply with the requirements of 37 C.F.R. §1.821 through 1.825 pertaining to the description of sequence identifiers, and ordered compliance with the rules. More particularly, sequences were listed in the specification without concomitantly reciting the related sequence identifiers set forth in the sequence listing. Applicants have amended claim 1 and the specification to rectify this omission. A marked version of the amendments is presented in Appendix A.

III. Rejection under 35 U.S.C. §112, first paragraph

The Examiner rejected claim 1 under 35 U.S.C. §112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one of skill in the relevant art that the inventors had possession of the claimed invention.

Briefly reiterating the Examiner's position, the Official Action states that "...there is no disclosure in the specification of a single method in which all the steps are carried out or in which all the reagents of the "set" of claim 1 are employed or of a single method employing a combination of these two methods..." (Official Action, page 5). Additionally, the Examiner states that the originally filed specification does not provide basis for the limitation "under stringent conditions". Applicants respectfully traverse these rejections.

A claimed invention need not be described *ipsis verbis* in order to satisfy the requirements of 35 U.S.C. §112. *Ex parte Holt*, 19 U.S.P.Q.2d 1211, 1213

(B.P.A.I. 1991). The Examiner's attention is directed to the specification page 36 lines 12-15 which specifically states that:

> "...possible to develop diagnostic processes based on the direct detection of AlaDH activity or, as already mentioned, on amplification of specific parts of the gene."

Additionally, the specification at page 37 lines 5-6 specifically provides that:

> "The disclosure also includes ***all conceivable combinations*** of the individual feature disclosed." (***Emphasis added***)

Given the above disclosure in the specification, Applicants specifically contemplated combinations of the enzyme test kit and a nucleic acid primer consisting of a DNA sequence set forth in claim 1.

Moreover, as indicated in the previous response, original claim 14 and indeed, original claim 15 both recited that the "...method according to claim 2 ***and/or*** claim 10. [Emphasis added.]" Thus, the original claims set forth a written description of a combination of the enzymatic kit of original claim 1 ***and*** the DNA components of original claim 9 to yield the diagnostic kit of present claim 1. Applicants have amended the term "set" to the phrase "diagnostic kit" in order to further clarify that the subject matter of claim 1 is a diagnostic kit comprising an enzyme kit of step (i) in combination with a nucleic acid of step (ii).

With respect to the rejection of the claim 1 for lack of written descriptive support for the term "high stringency conditions", Applicants have amended the claim to specific hybridization conditions. These conditions are specifically described at page 27 lines 3-5. As such, these claim elements are fully supported by the disclosure as filed.

Given the above discussion, the specification provides ample written description for claim 1 as amended and Applicants respectfully request that the rejection under 35 U.S.C. §112, first paragraph be withdrawn and the claims be reconsidered for allowance.

IV. Rejection under 35 U.S.C. §112, second paragraph

Claim 1 was rejected under 35 U.S.C. §112, second paragraph as being indefinite for failing to point out and distinctly claim the invention.

The Examiner objected to the term "set" as rendering the claim unclear. The components of claim 1, *i.e.*, an enzymatic kit of step (i) and a nucleic acid of step (ii) are combined together to yield a set or a kit that may be used in the diagnostic assays that are contemplated throughout the invention. In an effort to expedite the prosecution of the instant case, Applicants have amended claim 1 to recite a "diagnostic kit" (instead of "set") which comprises an enzymatic kit and a nucleic acid. Applicants believe that this amendment addresses the rejection, in the event that the Examiner wishes to discuss this matter further, Applicants respectfully solicit a telephone conference.

The Examiner objected to the limitation "the DNA sequence selected from the group consisting of..." stating that there was insufficient antecedent basis for the limitation. The amended claim recites "... ***a*** DNA sequence selected from the group consisting of ..." Applicants believe this amendment obviates the rejection.

The Examiner also objected to the claim for reciting "...sequences that are hybridizable therewith under stringent conditions..." because, according to the Examiner, neither the specification nor the prior art provides a clear definition of "stringent conditions". While Applicants maintain that, in light of the teachings of the specification, one of skill in the art would understand what is meant by "stringent conditions", in an effort to expedite the prosecution of the instant case, Applicants have amended the claim to recite specific hybridization conditions. This amendment obviates the rejection.

Given the above discussions, Applicants submit that the claim as amended is clear and definite in accordance with the requirements of 35 U.S.C. §112, second paragraph and request that the rejection be withdrawn and the claims be reconsidered for allowance.

V. The Rejection under 35 U.S.C. §103

The Examiner maintained the rejection of claim 1 under 35 U.S.C. §103(a) as allegedly obvious over Katsumata et al., U.S. Patent No. 5,559,016 ("the Katsumata patent") in view of Ahern, The Scientist 9:20 (1995) ("the Ahern publication"). It was the Examiner's position that the claim was not limited to particular probes but encompassed "partial sequences" of the recited sequences and that a single nucleotide could constitute such a partial sequence. Additionally, the Examiner

was concerned that the limitations of the term "consisting essentially of" were not defined in the specification, and as such the majority of the molecules encompassed by the claim do not possess the unexpected properties of the present invention. Applicants have amended the claim to remove recitation of "partial sequences thereof" and the term "essentially", and have also amended the claim to recite specific hybridization conditions. Applicants believe that with these amendments, the molecules encompassed by claim 1, do indeed possess the unexpected properties that Applicants have previously recited in the Response dated November 17, 2000 (incorporated herein by reference). More particularly, Applicants maintain that claim 1 encompasses specific nucleic acid fragments that have the unexpected property of being able to distinguish between pathogenic and non-pathogenic strains of *Mycobacteria*.

Given the above amendments, Applicants maintain that it would not be possible to use the nucleic acids disclosed in the Katsumata patent to distinguish between pathogenic and non-pathogenic organisms; thus, the nucleic acids taught by the art do not have the unexpected property of the nucleic acids of claim 1. Likewise, as Applicants have previously discussed, the inaccurate disclosure of Andersen et al., *Infection Immunity*, 60:2317 (1992) ("the Anderson publication") also does not teach the unexpected property of being able to distinguish between pathogenic and non-pathogenic strains of *Mycobacteria* and does not teach or suggest that it would have been possible to distinguish between non-pathogenic and pathogenic strains by means of such nucleic acids of the set of claim 1.

There is no suggestion or motivation to combine Katsumata with Ahern or indeed Anderson with Ahern to make the diagnostic kit of claim 1. Using hindsight afforded by the Applicants' own disclosure to identify disparate references that recite individual elements of the invention, without a suggestion or motivation to combine the references, to render the claimed invention obvious is impermissible, because the mere fact that the reference ***can*** be modified is not sufficient to establish a *prima facie* case of obviousness. *In re Mills*, 16 USPQ2d 1430 (Fed. Cir. 1990) (see MPEP 2143.01). The suggestion or motivation to combine the references must come from the art and not the Applicants' own disclosure (see MPEP 2143; *In re Vaeck*, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991)). In the present case, the only suggestion or motivation to produce the diagnostic kits for the diagnosis of *M. tuberculosis*, which kits comprises the elements

of step (i) and (ii) of claim 1 is to be found in the Applicants' own disclosure and not in the cited references.

Moreover, even if these references were fortuitously combined in the manner suggested by the Examiner, such a combination would not render obvious the claimed invention because the general discussion in Ahern regarding kits, or indeed the other references, does not suggest the unexpected property of the nucleic acids of the set of claim 1.

In light of the above discussions and amendment, Applicants respectfully request that the rejection under 35 U.S.C. §103 be withdrawn and the claims be reconsidered for allowance.

CONCLUSION

Claim 1 is believed to be allowable in view of the above amendments and remarks, and an early notice thereof is respectfully solicited.

Respectfully submitted,

MARSHALL, O'TOOLE, GERSTEIN,
MURRAY & BORUN

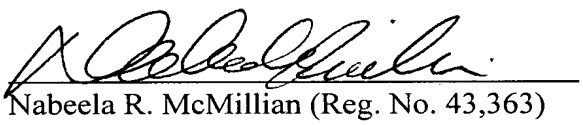
By: 

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EXHIBIT A

Marked Up Version of Amendment to Claim 1

1. (Twice Amended) A ~~set~~ diagnostic kit for the diagnosis of tuberculosis and other mycobacterial infections in humans and animals comprising:
(i) an enzymatic test kit for the determination of the activity of alanine dehydrogenase (E.C. 1.4.1.1), comprising L-alanine, nicotinamide adenine dinucleotide (oxidized form; NAD^+), phenazine methosulphate (PMS) and nitroblue tetrazolium chloride (NBT); and

(ii) a nucleic acid consisting ~~essentially~~ of ~~the~~ a DNA sequence selected from the group consisting of the following partial sequences of the alanine dehydrogenase gene of *M. tuberculosis*:

Name	Sequence	SEQ ID NO:	Orientation
AlaDH-F1	5'-ATGCGCGTCGGTATTCCG-3'	11	forward
AlaDH-F1+	5'-GCGCGTCGGTATTCCGACCG-3'	12	forward
AlaDH-F2	5'-GAGACCAAAAACAACGAA-3'	13	forward
AlaDH-F4	5'-GAATTCCCATCAGCAATCTTGCAGA-3'	14	forward
AlaDH-F5	5'-GCCCCGATGAGCGAAGTC-3'	15	forward
AlaDH-F6	5'-GGGGCCGTCCTGGTGCC-3'	16	forward
AlaDH-F7	5'-GACGTCGACCTACGCGCTGAC-3'	17	forward
AlaDH-R1	5'-CTCGGTGAACGGCACCCC-3'	18	reverse
AlaDH-R2	5'-GGCCAGCACGCTGGCGGG-3'	19	reverse
AlaDH-R3	5'-CACCCGTTCGGACAGTAA-3'	20	reverse
AlaDH-R4	5'-CGCGGCCGACATCATCGC-3'	21	reverse
AlaDH-R5	5'-GGCCGACATCATCGCTTCCC-3'	22	reverse
AlaDH-R6	5'-CGAGACTAATTTGGGTGCCTTGGC-3'	23	reverse
AlaDH-R7	5'-ATTTGGGTGCCTTGGC-3'	24	reverse
AlaDH-RM	5'-GGCGGCGAGTCGACCGGC-3'	25	reverse

~~partial sequences thereof~~ and sequences that are hybridizable therewith under ~~stringent conditions~~ the following conditions: annealing 2 minutes at 69°C and extension 3 minutes at 72°C at a 1.5mM concentration of $MgCl_2$, for the diagnosis of tuberculosis and other mycobacterial infections in humans or animals.

Please amend the specification as follows:

At page 4 please replace the table located between lines 4 through 19 inclusive, with the following replacement text:

--Name	Sequence	SEQ ID NO:	Orientation
AlaDH-F1	5'-ATGCGCGTCGGTATTCCG-3'	11	forward
AlaDH-F1+	5'-GCGCGTCGGTATTCCGACCG-3'	12	forward
AlaDH-F2	5'-GAGACCAAAAACAACGAA-3'	13	forward
AlaDH-F4	5'-GAATTCCCATCAGCAATCTTGCAGA-3'	14	forward
AlaDH-F5	5'-GCCCCGATGAGCGAAGTC-3'	15	forward
AlaDH-F6	5'-GGGGCCGTCCTGGTGCC-3'	16	forward
AlaDH-F7	5'-GACGTCGACCTACGCGCTGAC-3'	17	forward
AlaDH-R1	5'-CTCGGTGAACGGCACCCC-3'	18	reverse
AlaDH-R2	5'-GGCCAGCACGCTGGCGGG-3'	19	reverse
AlaDH-R3	5'-CACCCGTTCGGACAGTAA-3'	20	reverse
AlaDH-R4	5'-CGCGGCCGACATCATCGC-3'	21	reverse
AlaDH-R5	5'-GGCCGACATCATCGCTTCCC-3'	22	reverse
AlaDH-R6	5'-CGAGACTAATTTGGGTGCCTTGGC-3'	23	reverse
AlaDH-R7	5'-ATTTGGGTGCCTTGGC-3'	24	reverse
AlaDH-RM	5'-GGCGGCGAGTCGACCGGC-3'	25	reverse–

At page 14, please replace the table located between lines 2 and 17 with the following table:

Name	Sequence	SEQ ID NO:	Orientation
AlaDH-F1	5'-ATGCGCGTCGGTATTCCG-3'	11	forward
AlaDH-F1+	5'-GCGCGTCGGTATTCCGACCG-3'	12	forward
AlaDH-F2	5'-GAGACCAAAAACAACGAA-3'	13	forward
AlaDH-F4	5'-GAATTCCCATCAGCAATCTTGCAGA-3'	14	forward
AlaDH-F5	5'-GCCCCGATGAGCGAAGTC-3'	15	forward
AlaDH-F6	5'-GGGGCCGTCCTGGTGCC-3'	16	forward
AlaDH-F7	5'-GACGTCGACCTACGCGCTGAC-3'	17	forward
AlaDH-R1	5'-CTCGGTGAACGGCACCCC-3'	18	reverse
AlaDH-R2	5'-GGCCAGCACGCTGGCGGG-3'	19	reverse
AlaDH-R3	5'-CACCCGTTCGGACAGTAA-3'	20	reverse
AlaDH-R4	5'-CGCGGCCGACATCATCGC-3'	21	reverse
AlaDH-R5	5'-GGCCGACATCATCGCTTCCC-3'	22	reverse
AlaDH-R6	5'-CGAGACTAATTTGGGTGCCTTGGC-3'	23	reverse
AlaDH-R7	5'-ATTTGGGTGCCTTGGC-3'	24	reverse
AlaDH-RM	5'-GGCGGCGAGTCGACCGGC-3'	25	reverse